destruction was particularly found at the lateral plateau (48% lower). Interestingly, ASC-treatment had a protective effect on new cartilage and bone formation in the ligaments. At day 42, the surface percentage of the cruciate ligament which stained positive for proteoglycan deposition was decreased by nearly 43% in the ASC treated joints when compared to controls. In line with that, osteophyte formation in the medial collateral ligament was significantly reduced by 91% in ASC-treated animals compared to control. In contrast to early treatment, injection of the same dose of ASCs, 14 days after induction of OA only showed a small inhibiting effect on osteophyt formation and synovial activation when measured at day 42. Although cartilage destruction diminished with 28%, these values did not reach significance at that time-point.
Conclusions: Our study indicates that a single injection of ASCs into the knee joints of mice with collagenase-induced osteoarthritis prevents cartilage damage and the formation of bone structures within the ligaments, probably by inhibiting activation of the synovial macrophages.

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CHONDROGENIC AND IMMUNOPHENOTYPIC PROPERTIES OF MESENCHYMAL STEM CELLS FROM OSTEOARTHRITIS PATIENTS

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Purpose: Mesenchymal stem cells (MSCs) are a promising target for future cell-based therapies in osteoarthritis. In this context, cartilage tissue engineering is a major field of research, with effective cartilage repair being the ultimate objective. There is a controversy whether osteoarthritis and age affect the regenerative potential of MSCs. Also, in the last decade, it has become clear that MSCs are heterogeneous populations not only regarding their regenerative potential, but also regarding their surface markers. The aim of this study was to analyse the influence of osteoarthritis and age on growth parameters, immunophenotype and chondrogenic differentiation potential of human bone marrow derived MSCs.
Methods: MSCs were isolated from bone marrow of osteoarthritis patients (n=5, OA) and patients without clinical and radiological signs of osteoarthritis (n=5, non-OA) and expanded in different cell culture media. Flow cytometry analysis was performed for CD10, CD13, CD14, CD34, CD44, CD45, CD49, CD73, CD90, CD105, CD117, CD133, CD 140b, CD 166, CD271, CD340, Stro-1 and HLA-ABC. Chondrogenic differentiation was induced with chondrogenic medium in pellet culture. Chondrogenic differentiation potential was evaluated by a DMMB-assay and by semiquantitative analysis of GAG percentage (SafraninO/FastGreen staining). Statistical analysis as performed with analyses of variance (ANOVA).
Results: Both in the OA and the non-OA group, MSCs were negative for CD14, CD34 and CD45 and positive for CD13, CD44, CD73, CD90, CD105 and CD166. CD49, CD105, CD140b, CD146, CD340 and Stro-1 showed differences depending from the media applied, but no significant differences were observed between the OA and non-OA group. The expression of the MSC surface markers CD10, CD49 and CD146 showed high donor dependence while for these markers there was no significant difference between the OA and the non-OA group. Cell proliferation differed substantially between different culture media while the growth index parameters were similar in the OA and non-OA group. There was no difference in MSC chondrogenic potential between OA and non OA patients while the culture media had an important influence on chondrogenic differentiation.
Conclusions: Our findings add to the reports that negate the regenerative inferiority of MSCs from OA affected patients. Our experiments rather suggest that MSCs extracted from OA patients are an adequate source for cartilage tissue engineering, which is supported by the finding that MSC surface markers do not seem to be influenced by age or presence of OA. Our data also reflects that MSCs are heterogeneous regarding some of their surface markers and that culture conditions seem to have an important influence on both immunophenotype and chondrogenic potential.
In the long-term, understanding the potential of MSC heterogeneity and of culture conditions will hopefully lead to more efficient cartilage tissue engineering.

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LONG-TERM EFFICACY OF MESENCHYMAL STEM CELLS IMPLANTATION IN COMBINATION WITH TYPE I COLLAGEN MEMBRANE: A RAT EXPERIMENTAL MODEL OF ROTATOR CUFF TEARS.

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Purpose: The Supraspinatus tendon (SE) is an essential structure for the proper function of the rotator cuff frequently affected in rotator cuff tears. Common surgical procedures to repair SE lesions are usually adequate in the short term, but they are often unsatisfactory in the long term presenting a high rate of re-rupture. In this context, there is a need for new techniques allowing a more efficient repair. Regenerative medicine using mesenchymal stem cells (MSCs) offers a promising alternative. This study explore in a rat model the possible benefits of a treatment based on MSC-collagen membrane graft compared to conventional treatment (suture) or collagen membrane graft.
Methods: A chronic rotator cuff tear injury model was developed by unilaterally detaching the SE tendon of adult Sprague-Dawley rats. One month post-injury, the tendon was repaired by: a) Classical surgery, using single suture. b) suture + type I collagen membranes without cells; Membrane or c) suture + type I collagen membranes + $1x10^6$ allogeneic MSCs; (n=12; MSC-Membrane). Lesion was evaluated at 1 month, 2 months and three months post-injury by biomechanical criteria including "load-to-failure" measured (Newtons), Stifness (N/mm) and deformation (mm). The opposing and not injured shoulder was used as positive control after normalization. Non-parametric Mann-Whitney U test was used for statistical analysis, $p < 0.05$ was considered significant.
Results: Biomechanical properties (median [25%-75% percentil]) of tendon repair
Conclusions: We observed that implanting MSC-Membrane into surgically created tendon defects improved the strength and stiffness of the repaired tendon at three months, indicating that the reparation process ameliorated after long-term. This likely indicates that long-term efficacy is influenced by underlying mechanism improving the natural tendon repair.

	Months	n	Suture	n	Membrane	n	MSC-Membrane
Load to failure (N)	1	4	1.31 [1.19-1.69]	6	0.73 [0.35-1.23]	6	1.04 [0.77-1.22][b]
	2	4	1.22 [0.76-1.60]	4	0.99 [0.63-1.59]	5	1.11 [0.74-1.39]
	3	3	1.14 [0.28-1.29]	5	0.94 [0.84-1.27]	4	1.70 [1.27-1.79][a,b,c]
Total n		11		15		15	
Stiffness (N/mm)	1	4	1.20 [0.99-1.42]	6	0.62 [0.44-0.88]	6	0.63 [0.46-0.90]
	2	4	0.86 [0.49-0.91][c]	4	0.87 [0.53-2.15]	5	0.66 [0.47-1.05]
	3	3	0.70 [0.37-0.90][a]	5	0.91 [0.60-2.03]	4	1.16 [1.04-1.32] [a,b]
Total n		11		15		15	
Deformation (mm)	1	4	1.13 [0.77-1.40]	6	1.12 [0.84-1.66]	6	1.21 [0.83-2.02]
	2	4	1.53 [1.13-1.75]	4	1.01 [0.82-1.65]	5	0.98 [0.84-1.92]
	3	3	1.15 [0.68-1.68]	5	1.32 [0.54-2.30]	4	1.30 [0.84-1.42]
Total n		11		15		15	

[a] Statistically significant from same group repair.
[b] Statistically significant from Suture *vs* MSC-Membrane
[c] Statistically significant from Membrane *vs* MSC-Membrane